February 25, 1952

Dear Cavalli:

Your letters and Hfr culture just received. The latter is working nicely against W-1177 and also W-1177F+, so that I find no surprise, as you anticipated.

Hayes seems to have made a remarkable discovery; if you get this letter in time, I hope you will convey my respects to him. [May I tell you also that I was very much annoyed that he should have spoiled his contribution by his rash and unrestrained speculation about the role of lambda, and talking about "self-reproducing gametes"]. He may not know how much confusion this is going to cause, especially after our work on the Salmonella transduction is published. We have been taking great pains to keep clear the delineation of the E. coli and Salmonella work, and such premature speculations will not help at all.

Probably Hayes, yourself, and I have been doing this experiment all at the same time. The result is coming through now. The point is to establish a connection between Hayes' finding and our work on F-. As we have all known for some time, BM- F+ S^s x TLB_1- F- S^r (58-161 x W-1177) is moderately fertile even on streptomycin agar; whereas BM- F+ S^r x TLB_1- F- S^s is not. In my own observations, I had casually assumed that this was due to the linkage relations which give a preponderance of S^r protrotrophs in the first cross, S^s in the second, but I now agree that Hayes is quite correct. I have just compared these crosses with BM- F+ S^r x TLB_1- F+ S^s (W-677 F+) and BM- F- S^r x TLB_1- F+ S^s. Both of the latter <u>are</u> fertile on streptomycin agar! F+ therefore protects the fertility of S^s in the presence of streptomycin if the other parent is S^r. I am setting up other combinations of a similar design. If they agree, it will be necessary to postulate a second sexual function G, of which most or all stocks are G+, but which, in S^s cells is subject to inhibition by sm. Where I think Hayes has gone overboard is assigning detailed meanings to the second function, especially this business of "extruded-phage-stuck-to-cells". The picture does suggest that one parent must be F+, the other G+ for sexual reproduction to occur, but to refer to either as a male or female gamete is going far beyond the evidence. I will admit that it is more likely that the cytoplasmic structures are inhibited by sm, which would give G+ a male-like character, but there is no evidence still that is inconsistent with isogamous fusion. I see no point in making a fantasy of the story beyond the necessities of the evidence: at least in publication, Occam's razor should be applied generously.

Since my last letter, I have been thinking about the form of a publication. I am rather opposed to the idea of notes to Nature, and am very much in favor of writing a <u>joint</u> paper, rather than coincident notes. I have had some experience with the latter, and all it does is require other people either to give two references, or choose one. In view of the very gratifying sympathy of thought, objectives and experiment expressed in our correspondence, I would be very pleased at such an exposition of it. I am therefore proposing that we write a full paper together, and submit it to <u>Genetics</u>. This journal is now edited in this department, which makes many details much simpler. In particular, minor revisions such as might otherwise be troublesome in a transatlantic collaboration present no serious problem. If it will facilitate the proper clarification of our work in relation to Hayes, I would be amenable to a premonitory note in <u>Nature</u>, to accompany Hayes' if he is also agreeable. In order to minimize priority questions, I propose that you assume senior authorship for publication in an American journal, and the converse in a European. Mrs. Lederberg should, by rights, appear as a co-author in any full, (non-polemical!) exposition.

By the time you receive this, I will have (I hope) reached a definite conclusion on the sm experiments; perhaps you will as well. I have not yet written on this subject; I would prefer to mention it as succinctly as possible, still giving Hayes his due, and with as little speculative discussion as possible.

I am enclosing a draft that corresponds to my conception of the paper. As you can see, it is already of a respectable size, although no-one will accuse it of being padded. I send it only as a basis for discussion between us, and assuming that it will not hamper the free

expression of your side of it. I will admit readily that this version is strongly biased by my own viewpoint, but I have had so many experiences of a similar outlook that I do not anticpate any difficulty.

If we can put together a manuscript within a short time, it need not be letter-perfect to be submitted to Genetics (and reserve a place). If we are reasonably prompt, we can still find a place in the September issue. The editors have already expressed their interest. Entirely aside from any other pressures (real or imaginary), the writing of the draft convinced me that the time was appropriate. The SM-experiments now in progress were an afterthought, provoked by Hayes' paper in the Jan. 19 Nature which arrived a day or two ago, but do not seriously affect the structure of the paper, and should be described readily in half a page.

The whole subject seems to be coming alive. In some respects (not the most rapid advance of science) the somnolescence of the last few years may have been preferable.